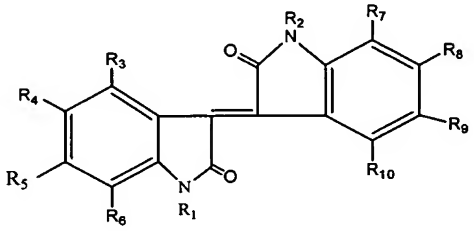
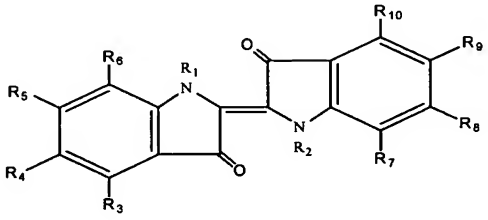
AMENDMENTS TO THE CLAIMS

The following claim listing replaces all prior claims version and listings in this application.

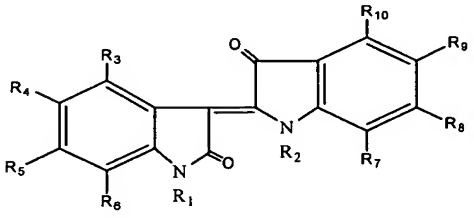
1. (original) A method of treating an inflammatory-related disease associated with cytokine expression levels, which comprises administering to an animal in need of such treatment at least one compound of formula (I), (II) or (III)



FORMULA (I)



FORMULA (II)



FORMULA (III)

wherein the compound is administered in an amount sufficient to treat the inflammatory-related disease by inhibiting pro-inflammatory cytokine expression or by stimulating anti-inflammatory cytokine expression, but the amount is less than sufficient to substantially inhibit cyclin dependent kinases;

R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and represent a hydrogen atom; a hydroxy group; a nitroso group; a nitro group; a monosaccharide; a disaccharide; a halogen atom; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties, nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms; a $-R_{11}R_{12}$ group, wherein R_{11} and R_{12} can be the same or different and represent a hydrogen atom, a straight-chain or branched-chain alkyl group having 1 to 18 carbon atoms which can additionally carry one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which can comprise one or more heteroatoms, or an acyl group, or R_{11} and R_{12} form together a ring having 2 to 6, optionally substituted, CH_2 groups; an azo group $-N=N-R_{13}$, wherein R_{13} represents an aromatic system which can be substituted by one or more carboxyl groups and/or phosphoryl groups, or a group selected from the group consisting of sugars, amino acids, peptides or steroid hormones; or R_1 and R_6, and R_2 and R_7, respectively, form independently from each other a ring together having 1 to 4, optionally substituted, CH_2 groups; and

R_1 and R_2 are the same or different and represent a hydrogen atom; a halogen atom; a hydroxy group; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties, nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms; a mono-, di- or trialkylsilyl group having 1 to 6 carbon atoms independently of each other in each instance in the straight-chain or branched-chain alkyl group; a mono-, di- or triarylsilyl group with substituted or unsubstituted aryl groups independently of each other in each instance; a $-NR_{17}R_{18}$ group, wherein R_{17} and R_{18} can be the same or different and represent a hydrogen atom, a straight-chain or branched-chain alkyl group having 1 to 18 carbon atoms which can additionally carry one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which can comprise one or more heteroatoms, or an acyl group; a methyleneamino group $-CH_2-NR_{17}R_{18}$, wherein R_{17} and R_{18} have the above definitions; a physiological amino acid residue bound to the nitrogen as an amide, substituted or unsubstituted monosaccharide, disaccharides or oligosaccharides; or a sugar, amino acid, peptide or steroid hormone.

2. (original) The method according to claim 1, wherein at least R_1 or R_2 is a monosaccharide, a disaccharide unsubstituted or substituted with one or more hydroxy moieties or carboxy moieties; a halogen; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties,

nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms.

3. (original) The method according to claim 2, wherein at least R_1 or R_2 is a group that increases the solubility of the compound.

4. (original) The method according to claim 2, wherein at least R_1 or R_2 is a tri-acetylated monosaccharide.

5. (original) The method according to claim 2, wherein at least R_1 or R_2 is a methyl group.

6. (original) The method according to claim 5, wherein R_1 or R_2 is an acetylated monosaccharide.

7. (original) The method according to claim 1, wherein the animal is a human being.

8. (original) The method according to claim 1, wherein at least two of the compounds are administered concurrently or sequentially.

9. (original) The method according to claim 1, wherein the compound is administered in combination with an anti-inflammatory agent.

10. (original) The method according to claim 9, wherein the anti-inflammatory agent is selected from the group consisting of: an analgesic; an antirheumatic agent; an gastrointestinal agent; a gout preparation; glucocorticoids; opthalmic preparation; respiratory agent; a nasal preparation; and a mucous membrane agent.

11. (original) The method according to claim 10, wherein the analgesic is selected from the group consisting of: naproxen, indomethacin, ibuprofen, ketorolac tromethamine, choline magnesium trisalicylate and rofecoxib; the antirheumatic agent is selected from the group consisting of: cyclosporine, sulfasalazine, valdecoxib, penicillamine and dexamethasone; the gastrointestinal agent is selected from the group consisting of: mesalamine, balsalazide disodium and olsalazine sodium; the gout preparation is sulindac;

the glucocorticoid is selected from the group consisting of: dexamethasone, dexamethasone phosphate, methylprednisolone acetate, hydrocortisone and hydrocortisone sodium phosphate; the nasal preparation is selected form the group consisting of beclomethasone dipropionate monohydrate, fluticasone propionate, triamcinolone acetonide, flunisolide, mometasone furoate monohydrate and budesonide; the opthalmic preparation is ketorolac tromethamine; the respiratory agent is nedocromil sodium; and the mucous membrane agent is selected from the group consisting of: alclometasone dipropionate, hydrocortisone butyrate, flurandrenolide, betamethasone valerate and clobetasol propionate.

12. (original) The method according to claim 2, wherein the disease is selected from the group consisting of arthritis, rheumatoid arthritis, arthritis, rheumatoid arthritis, an inflammatory bowel disease; psoriasis; multiple sclerosis; a neurodegenerative disorder; congestive heart failure; stroke; aortic valve stenosis; kidney failure; lupus; pancreatitis; allergy; fibrosis; anemia; atherosclerosis; a metabolic disease; a bone disease; a cardiovascular disease, a chemotherapy/radiation related complication; diabetes type I; diabetes type II; a liver disease; a gastrointestinal disorder; an ophthamological disease; allergic conjunctivitis; diabetic retinopathy; Sjogren's syndrome; uvetitis; a pulmonary disorder, a renal disease; dermatitis; HIV-related cachexia; cerebral malaria; ankylosing spondolytis; leprosy; anemia; and fibromyalgia.

13. (original) The method according to claim 12, wherein the neurodegenerative disorder is selected from the group consisting of: Alzheimer's disease and Parkinson disease; the inflammatory bowel disease is selected from the group consisting of: Crohn's disease or uncerative colitis; the gastrointestinal complication is diarrhea; the liver disease is selected from the group consisting of: an autoimmune hepatitis, hepatitis C, primary biliary cirrhosis, primary sclerosing cholangitis, or fulminant liver failure; the gastrointestinal disorder is selected from the group consisting of: celiac disease and non-specific colitis; the pulmonary disorder is selected from the group consisting of: allergic rihinitis, asthma, chronic obstructive pulmonary disease, chronic granulomatous inflammation, cystic fibrosis, and sarcoidosis; the cardiovascular disease is selected from the group consisting of: atheroscleotic cardiac disease, congestive heart failure and restenosis; and the renal disease is selected from the group consisting of: glomerulpnephritis and vasculitis.

14. (original) The method according to claim 13, wherein the disease is Crohn's disease or uncerative colitis.

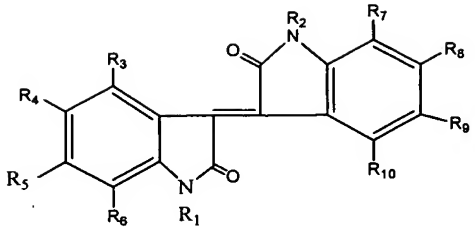
15. (original) The method according to claim 13, wherein the disease is psoriasis.

16. (original) The method according to claim 13, wherein the disease is Alzheimer's disease or Parkinson's disease.

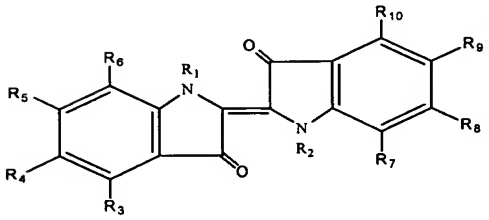
17. (original) The method according to claim 1 wherein the compound is administered at a concentration sufficient to inhibit cytokine IL-1α, β, IL-2, IL-3, IL-6, IL-7, IL-9, IL-12, IL-17, IL-18, TNF-α, LT, LIF, Oncostatin, or IFNc1α, β, γ.

18. (original) The method according to claim 1, where the compound is administered at a concentration sufficient to stimulate expression of cytokine IL-4, IL-10, IL-11, W-13 or TGFβ.

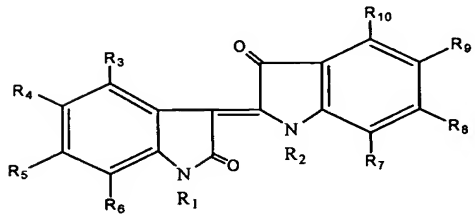
19. (original) A method of treating an inflammatory-related disease associated with cytokine expression levels in an animal, wherein the inflammatory-related disease being treated is selected from the group consisting of: an inflammatory bowel disease, rheumatoid arthritis; lupus; a gastrointestinal complication; chemotherapy/radiation related complication; diabetes type I; diabetes type II; a liver disease; a gastrointestinal disorder; an ophthamological disease; allergic conjunctivitis; diabetic retinopathy; Sjogren's syndrome; uvetitis; a pulmonary disorder, a renal disease; dermatitis; HIV-related cachexia; cerebral malaria; ankylosing spondolytis; leprosy; arthritis; multiple sclerosis; stroke; kidney failure; pancreatitis; an allergy; fibrosis; anemia; and fibromyalgia, the method comprising administering to an animal in need of such treatment at least one compound of formula (I), (II) or (III)



FORMULA (I)



FORMULA (II)



FORMULA (III)

wherein the compound is administered in an amount sufficient to treat the cytokine-induced inflammatory-related disease;

R_3, R_4, R_5, R_6, R_7, R_8, R_9, and R_{10} are the same or different and represent a hydrogen atom; a hydroxy group; a nitroso group; a nitro group; a monosaccharide; a disaccharide; a halogen atom; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties, nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms; a $-R_{11}R_{12}$ group, wherein R_{11} and R_{12} can be the same or different and represent a hydrogen atom, a straight-chain or branched-chain alkyl group having 1 to 18 carbon atoms which can additionally carry one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which can comprise one or more heteroatoms, or an acyl group, or R_{11} and R_{12} form together a ring having 2 to 6, optionally substituted, CH_2 groups; an azo group $-N=N-R_{13}$, wherein R_{13} represents an aromatic system which can be substituted by one or more carboxyl groups and/or phosphoryl

groups; or a group selected from the group consisting of sugars, amino acids, peptides or steroid hormones; or R_1 and R_6, and R_2 and R_7, respectively, form independently from each other a ring together having 1 to 4, optionally substituted, CH_2 groups; and

R_1 and R_2 are the same or different and represent a hydrogen atom; a halogen atom; a hydroxy group; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties, nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms; a mono-, di- or trialkylsilyl group having 1 to 6 carbon atoms independently of each other in each instance in the straight-chain or branched-chain alkyl group; a mono-, di- or triarylsilyl group with substituted or unsubstituted aryl groups independently of each other in each instance; a $-NR_{17}R_{18}$ group, wherein R_{17} and R_{18} can be the same or different and represent a hydrogen atom, a straight-chain or branched-chain alkyl group having 1 to 18 carbon atoms which can additionally carry one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which can comprise one or more heteroatoms, or an acyl group; a methyleneamino group $-CH_2-NR_{17}R_{18}$, wherein R_{17} and R_{18} have the above definitions; a physiological amino acid residue bound to the nitrogen as an amide, substituted or unsubstituted monosaccharide, disaccharides or oligosaccharides; or a sugar, amino acid, peptide or steroid hormone.

20. (original) The method according to claim 19, wherein the inflammatory bowel disease is Crohn's disease or uncerative colitis; the gastrointestinal complication is diarrhea; the liver disease is selected from the group consisting of: an autoimmune hepatitis, hepatitis C, primary biliary cirrhosis, primary sclerosing cholangitis, or fulminant liver failure; the gastrointestinal disorder is selected from the group consisting of: celiac disease and non-specific colitis; the pulmonary disorder is selected from the group consisting of: allergic rihinitis, asthma, chronic obstructive pulmonary disease, chronic granulomatous inflammation, cystic fibrosis, and sarcoidosis; and the renal disease is selected from the group consisting of: glomerulpnephritis and vasculitis.

21. (original) The method according to claim 19, wherein at least R_1 or R_2 is a monosaccharide, a disaccharide unsubstituted or substituted with one or more hydroxy moieties or carboxy moieties; a halogen; a hydrocarbyl group, or a functional hydrocarbyl group unsubstituted or substituted with one or more hydroxy moieties, carboxy moieties, nitroxy moieties, monosaccharides, disaccharides, amines, amides, thiols, sulfates, sulfonates, sulfonamides or halogens, wherein the hydrocarbyl has 1 to 8 carbon atoms.

22. (original) The method according to claim 21, wherein at least R_1 or R_2 is a group that increases the solubility of the compound.

23. (original) The method according to claim 21, wherein at least R_1 or R_2 is an acetylated monosaccharide.

24. (original) The method according to claim 21, wherein at least R_1 or R_2 is a methyl group.

25. (original) The method according to claim 19, wherein at least two of the compounds are administered concurrently or sequentially.

26. (original) The method according to claim 19, wherein the compound is administered in combination with an anti-inflammatory agent.

27. (original) The method according to claim 26, wherein the anti-inflammatory agent is selected from the group consisting of: an analgesic; an antirheumatic agent; an gastrointestinal agent; a gout preparation; glucocorticoids; opthalmic preparation; respiratory agent; a nasal preparation; and a mucous membrane agent.

28. (original) The method according to claim 27, wherein the analgesic is selected from the group consisting of: naproxen, indomethacin, ibuprofen, ketorolac tromethamine, choline magnesium trisalicylate and rofecoxib; the antirheumatic agent is selected from the group consisting of: cyclosporine, sulfasalazine, valdecoxib, penicillamine and dexamethasone; the gastrointestinal agent is selected from the group consisting of: mesalamine, balsalazide disodium and olsalazine sodium; the gout preparation is sulindac; the glucocorticoid is selected from the group consisting of: dexamethasone, dexamethasone phosphate, methylprednisolone acetate, hydrocortisone and hydrocortisone sodium phosphate; the nasal preparation is selected form the group consisting of beclomethasone dipropionate monohydrate, fluticasone propionate, triamcinolone acetonide, flunisolide, mometasone furoate monohydrate and budesonide; the opthalmic preparation is ketorolac tromethamine; the respiratory agent is nedocromil sodium; and the mucous membrane agent is selected from the group consisting of: alclometasone dipropionate, hydrocortisone butyrate, flurandrenolide, betamethasone valerate and clobetasol propionate.

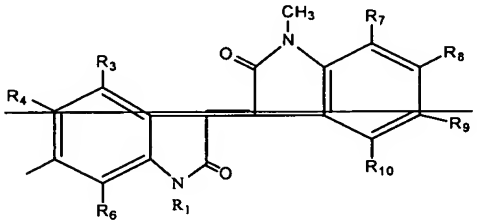
29. (original) The method according to claim 19 wherein the compound is administered at a concentration sufficient to inhibit cytokine IL-1α, β, IL-2, IL-3, IL-6, IL-7, IL-9, IL-12, IL-17, IL-18, TNF-α, LT, LIF, Oncostatin, or IFNc1α, β, γ.

30. (original) The method according to claim 19, where the compound is administered at a concentration sufficient to stimulate expression of cytokine IL-4, IL-10, IL-11, W-13 or TGFβ.

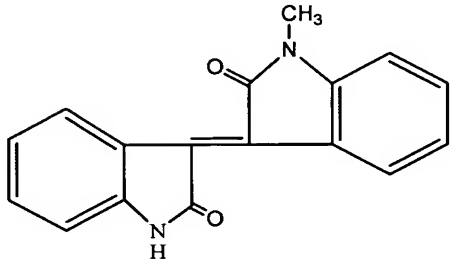
31. (original) A pharmaceutical composition for treating an inflammatory-related disease associated with cytokine expression levels in an animal comprising one or more compounds selected from isoindigo, indigo, indirubin, or a derivative thereof; an anti-inflammatory agent, and a pharmaceutically acceptable carrier, wherein the anti-inflammatory agent is selected from the group consisting of: an analgesic; an antirheumatic agent; an gastrointestinal agent; a gout preparation; glucocorticoids; opthalmic preparation; respiratory agent; a nasal preparation; and a mucous membrane agent.

32. (currently amended) The pharmaceutical composition according to claim [[29]] 30, wherein the analgesic is selected from the group consisting of: naproxen, indomethacin, ibuprofen, ketorolac tromethamine, choline magnesium trisalicylate and rofecoxib; the antirheumatic agent is selected from the group consisting of: cyclosporine, sulfasalazine, valdecoxib, penicillamine and dexamethasone; the gastrointestinal agent is selected from the group consisting of: mesalamine, balsalazide disodium and olsalazine sodium; the gout preparation is sulindac; the glucocorticoid is selected from the group consisting of: dexamethasone, dexamethasone phosphate, methylprednisolone acetate, hydrocortisone and hydrocortisone sodium phosphate; the nasal preparation is selected form the group consisting of beclomethasone dipropionate monohydrate, fluticasone propionate, triamcinolone acetonide, flunisolide, mometasone furoate monohydrate and budesonide; the opthalmic preparation is ketorolac tromethamine; the respiratory agent is nedocromil sodium; and the mucous membrane agent is selected from the group consisting of: alclometasone dipropionate, hydrocortisone butyrate, flurandrenolide, betamethasone valerate and clobetasol propionate.

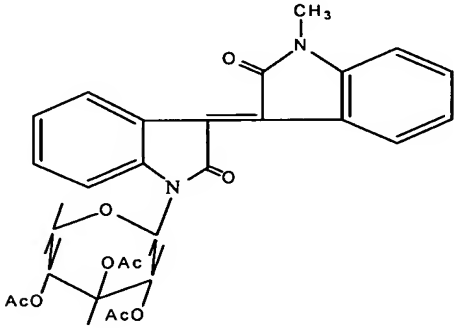
33. (Amended) The pharmaceutical composition according to claim 31, wherein the derivative is Meisoindigo, tri-acetylated glyco-Meisoindigo (pro-drug) or NATURA, shown as Formulas (IV), (V), and (VI) respectively,



~~FORMULA (IV)~~



FORMULA (IV)



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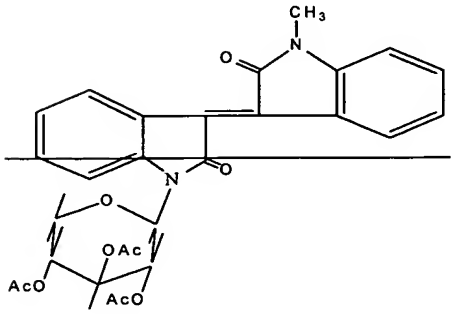
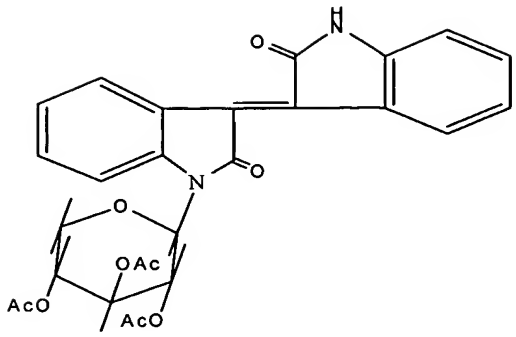


~~FORMULA (VI)~~



FORMULA (VI).

34. (original) The pharmaceutical composition according to claim 31, wherein the pharmaceutically acceptable carrier is an inert diluent.